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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/715,976	11/17/2003	Samuel Wadsworth	5121	5741

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EXAMINER	
WHITEMAN, BRIAN A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 12/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/715,976	WADSWORTH ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) *9-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11/17/03* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/12/05*
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Non-Final Rejection

Claims 1-16 are pending.

Election/Restrictions

Applicant's election of Group I (claims 1-8) in the reply filed on 11/4/05 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 9-16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/4/05.

Claim Objections

Claims 1-8 are objected to because of the following informalities: the claims read on a non-elected invention (ex vivo gene therapy). Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for practicing the method in an individual with either Type 1 diabetes or Type II diabetes and/or for reducing lipid accumulation in the liver, does not reasonably provide enablement for practicing the claimed method in a genus of individuals and reducing lipid accumulation in a genus of organs. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claimed method reads on administering to an individual a nucleic acid encoding a precursor GLP-1 linked to a heterologous signal sequence. The claimed method further reads on reducing lipid accumulation in a genus of organs. Thus, the claims are considered broad.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation (United States v. Technologies Inc., 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is required is not based upon a single factor, but rather a conclusion reached by many factors. These factors were outlined in Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in In Re Wands (see above).

The only intended use of the claimed method supported by the specification is for treating diabetes and non-alcoholic fatty liver disease (pages 5-6). The instant specification provides sufficient guidance for lowering plasma triglycerides and lipid accumulation in the liver of murine model of type 2 diabetes (page 51). However, the instant specification does not teach one skilled in the art how to practice the claimed invention in a genus of individuals and/or reducing lipid accumulation in a genus of organs. Claims 2 and 6 indicate that the claimed

method is broader than just practicing the method in an individual with diabetes. The invention involves one of the most complex areas of medicine/molecular biology (gene therapy). The instant specification and the prior art are absent for using GLP-1 to reduce lipid accumulation in a genus of organs. The skilled artisan would be further required to perform undue experimentation to determine which organs can be targeted for use in the claimed method. See MPEP 2164.08, which recites, "The focus of the examination inquiry is whether everything within the scope of the claim is enabled. The Federal Circuit has repeatedly held that the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation." See In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). It is noted that patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable (See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (19663, Stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion") Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.

In conclusion, the instant specification and claims coupled with the art of record, at the time the invention was made, do not provide sufficient guidance and/or factual evidence for practicing the full scope of the claimed invention. Given that reducing lipid accumulation in a genus of organs was unpredictable at the time the invention was made, and given the lack of

sufficient guidance as to using the method in a genus of individuals, one skilled in the art would have to engage in a large quantity of undue experimentation in order to practice the full breadth of the claimed invention based on the applicant's disclosure.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The limitation "activated GLP-1 reduces plasma triglyceride levels" in claim 1 and claims dependent therefrom and the limitation "activated GLP-1 reduces lipid accumulation in an organ" in claim 5 and claims dependent therefrom does not distinguish the claimed invention from the method taught in the prior art of record because the prior art uses the same material and method steps as recited in the instant claims. See MPEP 2112.02. See also In re King, 801 F.2d 1324, 23 USPQ 136 (Fed. Cir. 1986).

Claims 1-8 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Armentano et al. (Molecular Therapy, Vol. 7, S79, 2003). Armentano teaches delivering either a plasmid or adenovirus comprising GLP-1 chimeric expression vectors encoding a DDPIV-

resistant 31 amino acid peptide linked to a leader sequence required for secretion of GLP-1 to diabetic mice (Type II).

Claims 1-8 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Parsons et al. (Diabetes, Vol. 52, A130, 2003). Parsons teaches delivering either a plasmid or adenovirus comprising GLP-1 chimeric expression vectors encoding a 31 amino acid peptide linked to a leader sequence required for secretion of GLP-1 to diabetic mice (Type II).

Claims 1-8 are rejected under 35 U.S.C. 102(e) as being anticipated by Oh et al. (US 20030220274). Oh teaches a gene therapy method for treating diabetes (type II) comprising administering to the subject a nucleic acid encoding GLP-1 linked to a heterologous signal sequence (pages 3 and 11). Oh teaches the limitation in claims 3, 4, and 7 and 8 (pages 1 and 11).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 4-6, and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Staby (US 6444788). Staby teaches using GLP-1 for treating diabetes (column 1). Staby teaches an expression vector encoding GLP-1 peptide (column 19). Staby teaches to direct GLP-1 into the secretory pathway of cells, a secretory signal sequence is joined to the DNA (columns 19-21). The signal sequence may be normally associated with the peptide or may be from a gene encoding another secreted protein (column 20).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made, namely to produce an expression vector encoding a heterologous signal sequence linked to a GLP-1 and use the vector in a method for treating diabetes. One of ordinary skill in the art would have been motivated to make and use the vector in the method instead of administering GLP-1 because GLP-1 has a short half life in vivo and administering GLP-1 in a

vector would overcome the problem of the peptides short half life in vivo and because Staby teaches that one of ordinary skill in the art can use GLP-1 to treat diabetes.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 1, 3, 5, and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Staby (US 6444788) as applied to claims 1, 2, 4-6 and 8 above, and further in view of Oh et al. (US 20030220274).

Staby does not specifically teach using a viral vector in the method.

However, at the time the invention was made, viral vectors were well known in the art for delivering a nucleic acid in vivo as exemplified by Oh et al. (page 1).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Staby taken with Oh, namely to use a viral vector in the method taught by Staby. One of ordinary skill in the art would have been motivated to combine the teaching and use a viral vector instead of naked DNA because viral vectors have higher transfection efficiency than naked DNA (see Oh, page 1).

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is

appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-8 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 19-22 of copending Application No. 10/716,326. Although the conflicting claims are not identical, they are not patentably distinct from each other because both set of claims are directed to delivering a nucleic acid encoding a precursor glucagons-like peptide 1 (GLP-1) comprising mammalian GLP-1 linked to a heterologous signal sequence, wherein the precursor GLP-1 is cleaved in vivo.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

It is noted that an election/restriction was mailed on 11/2/05 for application '326 and applicants have yet to respond to the election/restriction.

Conclusion

It is noted that application 10/215,272 contains non-elected claims directed to claims being examined in the instant office action. Should the non-elected claims be rejoined with the elected invention in '272 a provisional double patenting will be applied to the pending claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, acting SPE – Art Unit 1635, can be reached at (571) 272-0811.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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